150/219 GC 1804

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1804

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	PENN-0065
Inventors:	Wolfe and Fraser
Serial No.:	08/393,066
Filing Date:	February 23, 1995
Examiner:	D. Crouch
Group Art Unit:	1804
Title:	Method of Delivering Genes to the Central Nervous System of A Mammal

I, **Jane Massey Licata**, Registration No. **32,257**, certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On this date: **May 8, 1997**

Jane Massey Licata

Jane Massey Licata, Registration No. **32,257**

BOX AF
Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

TRANSMITTAL LETTER

Transmitted herewith is an Appeal Brief, in triplicate.

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( ) The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).

(XX) Any filing fees under 37 CFR 1.16 including fees for presentation of extra claims.

Respectfully submitted,

Jane Massey Licata
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Date: **May 8, 1997**

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APPEAL BRIEF

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I. Real Party in Interest

The real party in interest is The Trustees of the University of Pennsylvania.

II. Related Appeals and Interferences

There are no related appeals or interferences.

III. Status of Claims

U.S. Application Serial No. 08/393,066, filed on February 23, 1995, is the subject of this appeal. This application is a continuation-in-part of Serial No. 08/020,177, which in turn was a file wrapper continuation of Serial No. 07/676,894.

This case was filed as a continuation-in-part in an earnest effort to facilitate the prosecution and allowance of this case. Appellants slightly revised the application to: (1) clarify the distinctions between the invention and the primary prior art reference, Dobson et al. (1989); (2) assist the Examiner in better understanding and characterizing the invention with respect to areas where there was obvious misunderstanding; and (3) assist the Examiner in evaluating the knowledge in the art at the time the invention was made and placing the invention in the appropriate context. A particular issue addressed was the difference between the central nervous system (CNS) and the peripheral nervous system (PNS). The Examiner's confusion about the difference between the CNS and the PNS was causing a significant misunderstanding of the invention. No additional subject matter was added to the case

which is now on appeal. Accordingly, this case has been treated during the course of its prosecution essentially as a file wrapper continuation case by both parties.

The Prosecution History of the '066 Application

In a first Office Action dated April 1, 1996, the specification and claims 1 through 9 were objected to under 35 U.S.C. §112, first paragraph, as failing to provide an enabling disclosure. Claims 1, 2, 5, and 6 were rejected under 35 U.S.C. §102(b) as being anticipated by Dobson et al. (1989). Claims 3, 4, 7, 8, and 9 were rejected under 35 U.S.C. §103 as being unpatentable over Dobson et al. (1989) in view of Nishimura et al. (1986).

A response to the first Office Action was filed on July 31, 1996. In this response, claim 1 was amended.

In a Final Office Action dated September 13, 1996, objection to the specification and rejection of claims 1 through 9 under 35 U.S.C. §112 were maintained. The Examiner again suggested that it was not apparent from disclosure that the method would sufficiently deliver a gene to the central nervous system such that the host would receive a benefit from such delivery. Claims 1, 2, 5, and 6 remained rejected under 35 U.S.C. §102(b) as being anticipated by Dobson et al. (1989). Rejection of claims 3, 4, 7, 8 and 9 under 35 U.S.C. §103 was also maintained over Dobson et al. (1989) in view of Nishimura et al. (1986).

A reply to the Final Rejection was filed on December 16, 1996 wherein claim 1 was amended.

In an Advisory Action mailed January 13, 1997, the pending §112, §102(b), and §103 rejections were maintained.

The final rejection of claims 1 through 9 under 35 U.S.C. §112, §102(b), and §103 is on Appeal. A copy of the claims involved in the Appeal is attached hereto as Appendix 1.

Placing The Status of the Claims in Context

The parent application, Serial No. 07/676,894 was filed on March 28, 1991 with nine claims. Claims 1 through 9 were rejected in the first Office Action dated February 26, 1992. The specification was objected to and claims 1 through 9 rejected under 35 U.S.C. §112, first paragraph, as failing to provide an enabling disclosure. Specifically, the Examiner suggested that an undue amount of experimentation would be required of the skilled artisan to implement the invention with a predictable degree of success. These comments related to the method for producing the plasmid. With respect to the claims (1 through 9), the Examiner suggested the disclosure was enabling only for claims limited to delivering a heterologous DNA sequence to mouse neuronal cells comprising administering to mice HSV-1, where said DNA sequence is regulated by the HSV-1 LAT promoter. The Examiner further suggested that undue experimentation would be required to extend the invention to other mammals. Claims 4, 5, and 7 were also rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter. The Examiner pointed to three phrases in the claims: "person", "modulating" and "genetically engineered". The Examiner rejected claims 1-3, 6 and 7 under 35 U.S.C. §102(b) as being anticipated by Ho et al. (1989). Finally, claims 4, 5, 8, and 9 were rejected under 35 U.S.C. §103 as being unpatentable over Ho et al. (1989).

A response to this first Office Action was filed on June 29, 1992 wherein amendments were made to the brief description of the drawings, the specification, and claims 4, 5, and 7.

In a Final Office Action dated September 22, 1992, the objection to the specification and rejection of claims 1 through 9 under 35 U.S.C. §112 were maintained. The rejection of claims 1-3, 6 and 7 under 35 U.S.C. §102(b) and claims 4, 5, 8, and 9 under 35 U.S.C. §103 were also maintained. Further, the amendments filed June 29, 1992 were objected to under 35 U.S.C. §132 because they introduced new matter into the specification.

On February 22, 1993 a continuation request was filed with the Patent Office under 37 C.F.R. §1.62 (FWC Request). The application, with claims 1 through 9, was accorded Serial No. 08/020,177 with a filing date of February 22, 1993.

A preliminary amendment was filed April 21, 1993 where the drawings, the specification, and the claims were amended. Claims 1 through 9 remained pending. The Appellants also addressed the Examiner's rejections under 35 U.S.C. §102(b), §103 and §112 in view of the amendments.

In the first Office Action dated October 27, 1993, the specification and claims 1 through 9 were rejected under 35 U.S.C. §112 because they failed to provide an enabling disclosure. Specifically, the Examiner suggested that the information provided in the specification failed to adequately enable a method of delivering genes to the central nervous system of animals and humans in general, and failed to enable the delivery and expression of therapeutic genes to alleviate a disease or condition. The Examiner also suggested a need to satisfy the requirements of enablement under 35 U.S.C. §112 by making a deposit of HSV-1 strain 17 under the terms of the Budapest Treaty because the strain was not publicly available. Claims 1 through 9 were further rejected under 35 U.S.C. §101 because the Examiner suggested they lacked patentable utility due to the unpredictable nature of the subject matter, i.e., delivery of genes to the central nervous system. Claims 1-3 and 6-8 were rejected under 35 U.S.C. §102(b) as being anticipated by Dobson et al. (1989). The Examiner also rejected claims 3, 4, 5, and 9 under 35 U.S.C. §103 as being unpatentable over Dobson et al. (1989).

A response to the first Office Action was filed on February 28, 1994. Claims 1 through 9 were cancelled and new claims 10 through 17 were added to more precisely define the invention and incorporate subject matter that had been cancelled.

In a Final Office Action dated August 26, 1994, claims 1 through 9 were cancelled and new claims 10 through 17 remained pending. The specification and claims 10 through 17 were rejected

under 35 U.S.C. §112 as failing to provide an enabling disclosure. The Examiner suggested that Appellants enabled only a method of delivering a DNA sequence to the brain of a mouse where the method comprises administration by corneal scarification of HSV-1 strain 17 containing a beta-glucuronidase cDNA sequence operatively linked to the LAT promoter. Appellants arguments were deemed persuasive to overcome the deposit requirement. The rejection of claims 10 through 17 under 35 U.S.C. §101 were maintained. Claims 10 through 17 also remained rejected under 35 U.S.C. §103 as being unpatentable over Dobson et al. (1989).

As this overview of the prosecution makes clear, there are two major areas of concern: the sufficiency of the disclosure concerning how the gene is delivered to the **central** nervous system (CNS), and whether prior art teachings concerning infection of the **peripheral** nervous system (PNS) with a viral vector are relevant prior art.

IV. Status of Amendments

The amendment filed on December 16, 1996 was entered upon filing of this appeal. A copy of the claims as amended in the response is attached hereto as Appendix 1.

V. Summary of Invention

The claimed invention is a method of delivering a gene of selected DNA sequence to the central nervous system (CNS) of a mammal by administering to that mammal a neurotropic virus, where

the virus contains a selected DNA sequence under the control of a promoter which permits expression of the gene during the latent infectious state of the virus. The ability to introduce a gene into the mammalian CNS *in vivo*, and altering the physiology of the CNS, is an important advance in the field of neurobiology, as well as in gene therapy for genetic diseases leading to neurological disorders. Neurotropic viruses, such as HSV-1, are useful vector systems because of features such as: 1) the ability to deliver a gene directly into post mitotic cells; 2) a wide host range; and 3) maintenance indefinitely in a latent state in postmitotic neuronal cells. The method of delivering genes to the central nervous system of a mammal would be suitable for application to a variety of neurological disorders (i.e., Lesch-Nyhan syndrome, mucopolysaccharidosis, other lysosomal storage diseases). Moreover, the method would be useful for delivery of a heterologous gene or selected DNA sequence that encodes a substance that alters **any** neurological function in a useful way, an example being the introduction of the tyrosine hydroxylase gene into Parkinson's disease patients to increase levels of dihydroxyphenylalanine (DOPA). Other examples of ways to use the method would include coding RNA designed to block expression of a gene and delivery of genes that encode compounds that bind receptors on neurons and alter cell function (e.g., blocking opiate receptors to modulate drug effects). Details in the specification demonstrate for the first time that a foreign gene can be delivered and expressed over a long period of time (i.e., greater than 4 months) in neurons of

the CNS following peripheral infection with a neurotropic virus. This long term expression of a foreign gene is an important advance that is particularly relevant to use of the claimed invention as a potential therapeutic. It has also been demonstrated that it is possible to correct a deficiency in biological function in cells of the CNS.

The method of the invention is described in detail at pages 9 through 20 of the specification. Information on the types and features of neurotropic viruses which support their use as vectors are discussed at pages 10-13 and page 15 (lines 1-31). Features of the promoters capable of expressing the heterologous gene during the latent infectious state from the selected neurotropic virus are described in detail on pages 13-14. Specific emphasis on the LAT promoter of HSV-1 is presented by way of illustration only. Description of the heterologous gene or selected DNA sequence suitable for delivery by the method of this invention is presented on page 15 (lines 33-37) and page 16 (lines 1-17); methods for cloning this sequence would be by any of a variety of methods known to those of skill in the art (see also Examples 1 and 2, pages 21-24). Delivery of cloned genes into targeted CNS neurons is described in detail on page 17 (lines 35-36) and pages 18-20. Examples 3-5 on pages 24-26 present *in vivo* evidence that a gene can be successfully delivered into targeted neurons of the CNS. More importantly, the expression of the delivered gene is not transient; the effect of the treatment was still evident more than 4 months after initial delivery of the gene in this mammal.

VI. Issues

The issues on appeal are whether (1) the specification and claims 1 through 9 are patentable under 35 U.S.C. §112, first paragraph; (2) claims 1, 2, 5, and 6 are patentable under 35 U.S.C. §102(b) over Dobson et al. (1989); and (3) claims 3, 4, 7, 8, and 9 are patentable under 35 U.S.C. §103 over Dobson et al. (1989) in view of Nishimura et al. (1986).

VII. Grouping of Claims

Claims 1 through 9 stand or fall together on the issue of whether the disclosure provides sufficient guidance under 35 U.S.C. §112, first paragraph concerning how to deliver a gene to the central nervous system of a mammal.

Claims 1, 2, 5, and 6 stand or fall together on the issue of anticipation over Dobson et al. (1989).

Claims 3, 4, 7, 8, and 9 stand or fall together on the issue of obviousness over Dobson et al (1989) in view of Nishimura (1986).

VIII. Arguments

A. Issue: Whether the Specification Provides Sufficient Guidance on How to Deliver Genes to the Central Nervous System of Mammals

1. The Enablement Requirement Under 35 U.S.C. §112, First Paragraph, Has Been Met

The enablement requirement refers to the requirement of 35 U.S.C. §112, first paragraph, that the specification describe how to make and how to use the invention. In accordance with MPEP

§2164, the invention that one skilled in the art must be enabled to make and use is that defined by the claims of the particular application or patent. In the present invention, the claims are drawn to delivery of selected DNA sequences to the central nervous system of a mammal comprising administering a neurotropic viral vector capable of infecting the central nervous system of a mammal. The selected DNA sequence of the vector is operatively linked to a selected promoter. Specific claims are drawn to the viral vector HSV-1, the LAT promoter, and the DNA sequence of beta-glucuronidase. The ability of this vector to deliver a gene successfully to the central nervous system of a mammalian species is clearly demonstrated and supported by the data provided in the specification (see particularly Examples 4 and 5 in the specification).

2. Therapeutic *Utility*, Not *Benefit*, is the Appropriate Standard for Patentability

The rejection of claims 1 through 9 under 35 U.S.C. §112, first paragraph, has been maintained. The Examiner suggests that the specification fails to provide adequate disclosure that the method of the claimed invention would sufficiently deliver a gene to the central nervous system such that a host would "receive benefit from such delivery". Although the Examiner admits that biologically active beta-glucuronidase is expressed when the DNA sequence for the enzyme operatively linked to the LAT promoter is contained in an HSV vector and is administered by corneal abrasion, the Examiner appears to doubt that such expression of the beta-

glucuronidase would have an effect on the host mammal or be an effective treatment for a beta-glucuronidase deficiency. According to the Examiner, delivery is read in light of the specification as gene therapy and there is no disclosure for delivery absent a **therapy**. Therefore, the Examiner has rejected the specification and claims 1 through 9 on the basis of failing to show a **therapeutic benefit** in a host. The Appellants respectfully disagree with the Examiner's analysis and conclusions.

Appellants respectfully point out that demonstration of therapeutic benefit is **not** a requirement of patentability. The case law is quite clear; Applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Thus, the Examiner's requirement that the specification demonstrate a therapeutic effect or a benefit to the host is improper.

Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881, 884 (CCPA 1980) and MPEP §2107.02. If one skilled in the art would accept the data provided as being reasonably predictive of utility in humans, evidence from these tests should be considered sufficient to support the credibility of the asserted utility. *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Krimmel*, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961); *Ex parte*

Krepelka, 231 USPQ 746 (Bd. Pat. App. & Inter. 1986). Further, in an earnest effort to advance the prosecution, Appellants even presented a Declaration by Dr. Laura Plunkett, one of skill in the art, which clearly stated that data provided in the instant specification are demonstrative of a pharmacological effect (delivery of a gene to the CNS of an animal and expression of that gene) and thus, **therapeutic utility** (see specifically paragraphs 3 and 4 of Dr. Plunkett's declaration attached hereto as Appendix 2). Thus, contrary to the Examiner's suggestion, data provided in the instant specification provide one of skill in the art with assurance that the invention delivers genes to the central nervous system in accordance with the claims. The teachings of the specification can be used in conjunction with general knowledge in the art establishing strategies for use of this delivery system in humans (this is also supported in paragraph 4 of Dr. Plunkett's Declaration; see Appendix 2). Further, confirmation of this approach can even be found in standard textbooks of medical pharmacology (e.g., *Goodman & Gilman's* The Pharmacological Basis of Therapeutics, 1996), where an entire chapter of text in the *General Principles* section is devoted to gene therapy; copy attached hereto as Appendix 3, for convenience). Clearly, pharmacologists view gene therapy as another tool for drug delivery that has reached the level of acceptance as one of many tools in pharmacology. Accordingly, the instant specification must be viewed as enabling one of skill in the art to make and use the invention to deliver genes to the central nervous system as claimed. It is not

appropriate to dismiss the data and teachings of the specification because one is simply skeptical of the idea of gene therapy when there is objective evidence of successful application of the claimed method.

3. Working Examples of Every Embodiment of the Claimed Invention are Not Required Under Patent Law

The Examiner also suggests that other neurotropic viruses and routes of delivery have not been shown to have a therapeutic effect in a host. As discussed above, however, any requirement for a demonstration of therapeutic effect is legally improper. Working examples of every embodiment of the claimed invention are clearly not required. See MPEP §2164.02. The determination of the propriety of such a rejection involves a two stage inquiry. The first stage is to determine how broad the claim is with respect to the disclosure. The second inquiry is to determine if one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation. The specification clearly teaches other neurotropic viruses at page 10, and routes of administration at page 20, which can be used in the present invention. As discussed in paragraph 3 of Dr. Plunkett's Declaration, experimental data provided in Example 4 and 5 of the specification, wherein the vector was administered through corneal abrasion, indicate to one of skill in the art that other peripheral routes of administration would be effective. Thus, Appellants have shown that the teachings of the specification are commensurate with the scope of the claims. The Examiner, however, has provided no

reasonable basis for her suggestions. The requirements of 35 U.S.C. §112, first paragraph have been met as a matter of scientific and legal fact. Therefore, Appellants respectfully request reconsideration and withdrawal of this rejection.

B. Issue: Whether the invention is anticipated by the cited art

1. Rejection of Claims 1, 2, 5, and 6 under 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 2, 5, and 6 as being anticipated by Dobson et al. (1989). The Examiner continues to suggest that Dobson et al. teach delivery of rabbit beta-globulin gene to the **central nervous system** (CNS) of an animal. In the Final Rejection (dated September 13, 1996) the Examiner suggested that the arguments presented by the Appellants to overcome this rejection of claims were not persuasive because the statement in the claims "capable of infecting the central nervous system" does not preclude the herpes virus from infecting another cell, such as a peripheral neuron, as a result of this method. Using this logic, the Examiner suggests that Dobson et al. (1989), which teach **peripheral** nervous system delivery of a gene with the herpes virus vector, would anticipate the claimed invention. As a result, in the response to the Final Rejection (dated December 13, 1996) the Appellants amended claim 1 to remove the phrase "capable of" to make clear that the neurotropic viral vector **infects** the **central** nervous system (claim 1 now has the phrase "which infects" instead of "capable of"). Even with this amendment to the claims, the

Examiner has maintained the rejection under 35 U.S.C. §102(b). Appellants therefore respectfully disagree with the Examiner's analysis and conclusions.

2. Dobson et al. (1989) teach delivery of beta-globulin gene only to peripheral neurons

Appellants disagree with the Examiner's characterization and analysis of Dobson et al. (1989). The reference teaches only **peripheral** nervous system infection with herpes virus and expression of beta-globulin in **peripheral** neurons. In an earnest effort to advance the prosecution, Appellants even provided a Declaration by one of skill (Appendix 2) which made clear in paragraph 5 that Dobson et al. do **not** teach delivery of a gene to the CNS. As the Declarant states,

> the fact that someone has shown the ability of a viral vector to infect cells in the peripheral nervous system (as in Dobson et al. 1989) would not imply to one of skill that the same vector would infect and successfully express genes in cells of the CNS.

Appellants strongly disagree and have shown that what does convince one of skill data that presented in the specification (Examples 4 and 5), where the subject of the invention is capable of CNS infection and successful gene expression in a mammal. Accordingly, the Examiner's comments and conclusions are simply incorrect as a matter of scientific fact and legally improper.

2. The requisite criteria to establish anticipation have not been met

The case law and the MPEP are quite clear. To anticipate a claim, the reference must teach every element of the claim. See MPEP §2131 and *Verdegall Bros. v. Union Oil Co. of California* 2 USPQ2d 1051 (Fed. Cir. 1987). Thus, the relevant question to ascertain whether Dobson et al. is an anticipating reference is whether this reference teaches every element of the instant claim, **not** whether the herpes virus may infect other cells besides those of the CNS, as indicated by the Examiner. Claim 1 which recites that the neurotropic viral vector **successfully infects** the **central** nervous system (CNS) is completely distinct from Dobson et al., where the **peripheral** nervous system (PNS) is infected with a viral vector. The rejection under 35 U.S.C. §102(b) therefore must be withdrawn.

C: Whether the invention is obvious in light of the cited art

The rejection of claims 3, 4, 7, 8, and 9 under 35 U.S.C. §103 as being unpatentable over Dobson et al. (1989) in view of Nishimura et al. (1986) was also maintained. The Examiner suggested that Dobson et al. teach delivery of the rabbit beta-globulin gene to the CNS. However, this suggestion is incorrect as discussed above (Section B.1). Further, the Examiner suggests that as Nishimura teaches the DNA sequence for beta-glucuronidase, it would have been within the scope of skill of the ordinary artisan at the time of the instant invention to insert his DNA sequence

into recombinant HSV-1 vectors as described by Dobson et al. (1989). The Examiner suggests that motivation is offered by Dobson et al. (1989), where it is stated that HSV-1 is a vector for the transfer of genes to neurons.

As pointed out in Section B, *supra*, Dobson et al. (1989) teach that HSV-1 is a vector for transfer of genes to neurons of the **peripheral** nervous system, i.e., neurons which are located **outside** of the CNS. In contrast, the claims of the instant invention are drawn to a method of delivering genes to neurons **within** the CNS. It must be remembered that the term "neuron" does not imply location within the CNS, but instead applies to nervous tissue in both the peripheral and central nervous systems. Appellants also point to the amendments to the claims clarifying that the neurotropic viral vector **infects** the CNS. Spinal ganglia, the location of the neurons examined by Dobson et al. (1989), are **not** tissues of the CNS. They differ from the CNS in that they are protected from exposure to foreign compounds, such as viruses, by the blood-brain barrier. This is also supported by Declaration of Dr. Plunkett (paragraph 5, Appendix 2). Accordingly, the mere fact that Dobson et al. (1989) were able to demonstrate delivery of a gene to the peripheral nervous system does not suggest to one of skill in the art that a similar vector could be used to deliver a gene to the CNS. Therefore, the teachings of Dobson et al. (1989) alone, or in combination with Nishimura et al. (1986), which merely teach a gene sequence, fail to provide one of skill in the art with a reasonable expectation of success that an HSV-1 vector would

deliver a gene to the CNS. As a result, this combination of references can not render the instant invention obvious. It is therefore respectfully requested that the rejection of claims 3, 4, 7, 8, and 9 under 35 U.S.C. §103 be withdrawn.

IX. Conclusion

The Examiner has failed to establish a *prima facie* case of anticipation or obviousness for the method of the instant invention. In fact, the references cited by the Examiner clearly fail to provide any relevant teaching of the present invention and suggest a fundamental misunderstanding of the invention. Peripheral administration of HSV-1 vector and demonstration of delivery of a gene through that vector to the **peripheral** nervous system does not suggest to one of skill that delivery to the **central** nervous system, following peripheral administration, would be successful. In an earnest effort to advance the prosecution, Appellants have even taken the initiative and provided a sworn statement from a disinterested expert that shows that the Examiner's analysis and conclusions are scientifically unsound. The Examiner has provided no reasonable basis in support of her position and these rejections are, therefore, legally improper. Accordingly, it is requested that the rejection of claims under 35 U.S.C. §102(b) and §103 be withdrawn and this case allowed.

Moreover, the requirements of 35 U.S.C. §112 have clearly been met. Combining what is known in the art concerning delivery of genes through viral vectors such as HSV-1 and what is taught in the

specification (see Examples 4 and 5, as well as pages 11-20 of the specification), one of skill in the art could use the claimed invention. It is not appropriate to dismiss the data and teachings of the specification because one is simply skeptical of the idea of gene therapy when there is objective evidence of successful application of the claimed method. Appellants respectfully point out that the claims are limited to successful infection of a gene *in vivo* and expression of that gene, which has been clearly demonstrated in this case. Accordingly, it is requested that the objection to the specification and the rejection of claims under 35 U.S.C. §112 be withdrawn and this case be allowed.

Respectfully submitted,

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Date: **May 8, 1997**

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